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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/534,010	05/05/2005	Theodore L. DeWeese	59564(71699)	2794

7590 07/18/2008

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EXAMINER	
CHONG, KIMBERLY	
ART UNIT	PAPER NUMBER
1635	

MAIL DATE	DELIVERY MODE
07/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/534,010	DEWEESE ET AL.	
	Examiner	Art Unit	
	KIMBERLY CHONG	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 April 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,23 and 24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,23,24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application/Amendment/Claims

Applicant's response filed 04/08/2008 has been considered. Rejections and/or objections not reiterated from the previous office action mailed 01/08/2008 are hereby withdrawn. The following rejections and/or objections are either newly applied or are reiterated and are the only rejections and/or objections presently applied to the instant application. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

With entry of the amendment filed 04/08/2008, claims 1-3 and 23-24 are pending in the application. Applicant has canceled claims 4-22, and 25-51.

New Claim Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The claim amendments necessitate this written description rejection.

The claims are drawn to a method of killing a tumor cell comprising contacting the cell with at least one siRNA wherein the siRNA is encoded by a nucleic acid molecule that is at least 85% identical to SEQ ID No. 4 or a portion thereof, specific for a DNA repair protein. A reasonable interpretation of "at least 85% identical to SEQ ID No. 4 or a portion thereof" includes any siRNA that is encoded by a nucleic acid sequence that is 85% identical to any portion of SEQ ID No. 4. Therefore, the claims embrace the use of a broad genus of siRNA that are specific for any DNA repair protein in a method of killing tumor cells.

To satisfy the written description requirement, MPEP §2163 states, in part "...a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor had possession of the claimed invention." Moreover, the written description requirement for a genus may be satisfied through sufficient description of a representative number of species by "...disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between functional and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus."

The specification as filed discloses a siRNA-encoding nucleic acid sequence having SEQ ID No. 4 recited as Oligo-A in Figure 15. The specification fails to provide adequate written description of a representative number of species that are commensurate in scope with the breadth of the instant invention. The specification fails

to disclose an adequate number of representative species in sufficient detail that one of skill in the art can immediately envision the genus of said siRNA such that one of skill can reasonably conclude that Applicant had possession of the claimed invention.

The disclosure does not provide any written description of siRNAs that can be encoded by nucleic acid sequences that are at least 85% identical to any portion of SEQ ID No. 4 wherein the siRNA are specific for a DNA repair protein and are capable of silencing gene expression of the DNA repair protein and killing a tumor cell. The specification as filed does not provide any specific guidance that would lead one of skill in the art to know what sequence having least 85% identical to any portion of SEQ ID No. 4 could encode a siRNA such that the siRNA would target a DNA repair protein and silence gene expression of said DNA repair protein that would lead to the death of tumor cells. Moreover, even post-filing, the state of the art clearly highlights the obstacles encountered in designing effective siRNA. As evidenced by Ryther et al. (Gene Therapy 2005, Vol. 12, pages 5-11), for all siRNAs design of effective siRNAs needs to be validated to obtain siRNA specific for a particular target (see page 8). MPEP §2163 states, in part "A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process." Therefore, because siRNAs need to be designed and tested to obtain effective siRNAs that specifically target a desired gene and silence expression of said gene, one of skill in the art would not know which sequence of the broad genus of siRNA-encoding nucleic acid sequences being at least 85% identical to SEQ ID No. 4 or any portion thereof that is

instantly claimed would provide the necessary function of targeting a DNA repair protein and killing tumor cells.

Furthermore, MPEP §2163 states, in part: "[A] patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. A patentee will not be deemed to have invented species sufficient to constitute the genus by virtue of having disclosed a single species when ... the evidence indicates ordinary artisans could not predict the operability in the invention of any species other than the one disclosed. *In re Curtis*, 354 F.3d 1347, 1358, 69 USPQ2d 1274, 1282 (Fed. Cir. 2004).

Therefore, in the instant application, Applicants have not shown possession of the entire claimed genus of siRNA that can be encoded by a nucleic acid sequences that is at least 85% identical to any portion of SEQ ID No. 4 wherein the siRNA are specific for a DNA repair protein and are capable of silencing gene expression of the DNA repair protein and killing a tumor cell.

Applicants are reminded that the written description requirement is separate and distinct from the enablement requirement. *In re Barker*, 559 F.2d 588, 194 USPQ 470 (CCPA 1977), cert. denied, 434 U.S. 1064 (1978); *Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d 1555, 1562, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991).

Response to Applicant's Arguments

Re: Drawings

The drawings filed on 05/05/2005 remain objected to under 37 CFR 1.83(a) for the reasons of record. Applicants indicate they are preparing new drawings and will submit such drawings under a separate cover.

Re: Claim Rejections - 35 USC § 112

The rejection of record of claims 1-3 and 23-24 under 35 U.S.C. 112, first paragraph, is maintained for the reasons of record in the Office action filed 01/08/2008.

Applicant's arguments filed 04/08/2008 have been fully considered but they are not persuasive. Applicant argues the specification provides detailed teaching regarding the use of adenoviral vectors for the expression of siRNA and the field of adenoviral based gene therapy was well-developed at the time the instant application was filed. These arguments are not persuasive. First, the claims are not drawn to adenoviral gene delivery. The claims are drawn to method of killing a tumor cell comprising contacting a siRNA targeted against a DNA repair protein and the use of an adenoviral vector is not recited in the instant claims. Secondly, even with the use of an adenoviral gene delivery system, there is still a high level of unpredictability in the siRNA art for therapeutic in vivo applications and given there is no guidance in the specification that would be considered enabling for the breadth of the claimed subject matter and there is no working embodiment of in vivo delivery of siRNA targeted to a DNA repair protein such that siRNA is shown to enter the cell, target the DNA repair protein and decrease

expression of said protein, the rejection is thus maintained. The scope of the claims in view of the specification as filed together do not reconcile the unpredictability in the art to enable one of skill in the art to make and/or use the claimed invention. Without further guidance, one of skill in the art would have to practice a substantial amount of trial and error experimentation, an amount considered undue and not routine, to practice the instantly claimed invention.

Re: Claim Rejections - 35 USC § 102

The rejection of claim 1 under 35 U.S.C. 102(b) as being anticipated by Collis et al. (Nucleic Acids Research 2001, Vol. 29, No. 7: 1534-1538) is withdrawn.

Re: Claim Rejections - 35 USC § 103

The rejection of claims 1-3 as being rejection under 35 U.S.C. 103(a) as being unpatentable over Fan et al. (Cancer Gene Therapy 2000, Vol. 7, No. 10: 1307-1314), Hammond et al. and Tuschl et al (WO 02/44321) is maintained for the reasons of record.

Applicant's arguments filed 04/08/2008 have been fully considered but they are not persuasive. As amended the claims are drawn to a siRNA encoded by a nucleic acid sequence that is at least 85% identical to SEQ ID No. 4 or a portion thereof. Fan et al. teach generation of an antisense molecule from the transcriptional start domain of the human ATM gene having nucleotides 188 to 445 which comprises nucleotides 395 to 445 of SEQ ID No. 4 (see Figure 15, Oligo-A). Fan et al. teach generation of an

antisense compound from the transcriptional start domain region of the human ATM DNA repair gene that is 100% identical to a portion of SEQ ID NO. 4. Fan et al. teach ATM antisense from the transcriptional start domain are capable of down regulating expression of the ATM DNA repair protein when administered to human prostate cancer cells and as discussed in the rejection of record, one of ordinary skill in the art would have wanted to generate a siRNA molecule to this region of an ATM gene to more efficiently inhibit expression of DNA repair protein in a method of killing a tumor cell given siRNAs were well known in the art at the time of the instant filling to be more efficient at silencing gene expression than antisense molecules.

Thus the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made and the rejection of record is maintained.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Kimberly Chong whose telephone number is 571-272-3111. The examiner can normally be reached Monday thru Friday between 7-4 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz can be reached at 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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KC
Examiner AU1635

/Sean R McGarry/
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